abbreviations, "FF" and "CF," as suggested by the Examiner. Claims 1-6, 17-28 and 30-28 have been withdrawn from the consideration as non-elected. Applicant also supplement an abstract as requested by the Examiner. A Sequence Listing to comply with 37 CFR §§1.821-1.825 are submitted concurrently herewith.

II. Rejection under 35 USC §112, Second Paragraph

The Examiner has rejected claims 7-16 and 29 as indefinite. More specifically, the Examiner objected to the term, "phophotopeptide," in claim 7 as misspelled, to the term, " HPO_4, " in claim 9 as non-existing form, and to the abbreviations, "PP" and "CP" in claims 12 and 13 for lack of definition. As explained above, claims 29 has been cancelled. Moreover claims 7, 9, 12 and 13 have been amended herein to attend the Examiner's concerns. Accordingly, Applicant respectfully requests withdrawal of this rejection.

III. Rejection under 35 USC §102(e) or (b)

The Examiner has rejected claims 7-9 as anticipated by US Patent No. 5,981,475 to Reynolds (" '475 Patent") or by Reynolds, *J. Dent. Res.* 74(6) 1272, 1995 ("Reynolds I"). The Examiner contends that each of these documents teaches a mixture of calcium phosphate and a peptide comprising the sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu. Furthermore, the Examiner has rejected claims 7-11 as anticipated by Reynolds, *Proceedings of the Nutrition Society of Australia* 19, 95-102, 1995 ("Reynolds II") or Holt, asserting that these publications teach at least one of the claimed sequences together with calcium phosphate. Applicant respectfully traverses these rejections.

At the outset, Applicant would direct the Examiner to amended claim 7, which prescribes an "amorphous calcium phosphate or the derivative thereof [that] is alkaline."

The claimed invention relates to a stable, amorphous calcium phosphate complexes produced by stabilizing an alkaline phase of calcium phosphate with casein phosphopeptides ("CPP"). For example, the alkaline phase of calcium phosphate is prepared under pH 9.0. See page 10, lines 7-10 and Example 1 of the specification. The use of the alkaline phase of calcium phosphate in the present application not only

Pg 12

prevents from precipitation of calcium phosphate out of its solution but also enhances binding affinity to phosphopeptide, thereby providing superior anticariogenic agent with increased calcium bioavailability. Thus, the claimed invention reflects a finding that the form of the amorphous calcium phosphate phase, stabilized by CPP, can vary with pH, as does calcium phosphate binding and efficacy

The specification highlights an appreciation in the prior art that preparing such stable complex is by no means straightforward, because amorphous calcium phosphate has a tendency to precipitate rapidly out of solution and transform into crystalline hydroxyapatite (HA). The resulting product has limited value and bioavailability. Furthermore, an acidic phase of calcium phosphate ($CaHPO_4$), while more soluble than HA, is known for poor binding affinity to phosphopeptide and poor localization ability at the tooth surface, both factors that limit anticariogenic activity. That is, at acidic pH values (below 7.0) and neutral pH values (pH 7.0), the efficacy and binding of the amorphous calcium phosphate phase stabilized by the CPP is significantly less than that stabilized at alkaline pH.

However, none of the cited publications suggests use of alkaline phase of calcium phosphate. The '475 patent filed by the Applicant, as well as Reynolds I and II, Applicant's own publications, disclose stabilization of calcium phosphate using the CPP. But the preparation of the CPP-stabilized phase in these references is limited to neutral phase, *i.e.*, pH 7 or pH 7.4. Moreover, the '475 patent only teaches adjusting pH to 7.0 with NaOH and $CaCl_2$ to prepare calcium CPP. See column 3, line 1. In addition, Holt is limited to the preparation under acidic conditions, from about 5.5 to 6.7.

Furthermore, the cited prior art does not implicate the use of alkaline phase of calcium phosphate to produce a superior anticariogenic agent with improved efficacy and bioavailability.

It is axiomatic that a reference, to be anticipatory, must expressly describe each and every element of the claimed invention. Therefore, none of the cited reference substantiates an anticipation of the presently claimed invention. Accordingly, with of the subject rejection is respectfully requested.

In view of the foregoing, Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if there are any issues that the Examiner believes could be resolved through a further exchange.

Respectfully submitted,

Date April 2, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Marked up replacement paragraph:

Page 2 paragraph 2.

Preliminary investigations determined that tryptic casein phosphopeptides contributed to the anticariogenic activity and this was made subject of US Patent No. 5,015,628. In particular, peptides Bos α_{s1}-casein X-5P (f59-79) [[1]](SEQ ID NO: 1), Bos β-casein X-4P (fl-25) [[2]](SEQ ID NO: 2), Bos α_{s2}-casein X-4P (f46-70) [[3]](SEQ ID NO: 3) and Bos α_{s2}-casein X-4P (fl-21) [[4]](SEQ ID NO: 4) were disclosed in US Patent 5,015,628 as follows:

[[1]](SEQ ID NO: 1) Gln^{59}-Met-Glu-Ala-Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys^{79}. α_{s1}(59-79)

[[2]](SEQ ID NO: 2) Arg^{1}-Glu-Leu-Glu-Glu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg^{25}. β(I-25)

[[3]](SEQ ID NO: 3) Asn^{46}-Ala-Asn-Glu-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys^{70}. α_{s2}(46-70)

[[4]](SEQ ID NO: 4) Lys^{1}-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys^{21}. α_{s2}(1-21)

Page 4 paragraph 1.

In one aspect, the invention provides a stable calcium phosphate complex, comprising amorphous calcium phosphate or a derivative thereof stabilized by a phosphopeptide, wherein said phosphopeptide comprises the sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu-(SEQ ID NO: 5).

Page 4 paragraph 3.

The phosphopeptide (PP) may be from any source; it may be obtained by tryptic digestion of casein or other phospho-acid rich proteins such as phosphitin, or by chemical or recombinant synthesis, provided that it comprises the core sequence –

Ser(P)-Ser(P)-Ser(P)-Glu-Glu-(SEQ ID NO: 5). The sequence flanking this core sequence may be any sequence. However, those flanking sequences in α_{s1}(59-79) [[1]](SEQ ID NO: 1), β(1-25) [[2]](SEQ ID NO: 2), α_{s2}(46-70) [[3]](SEQ ID NO: 3) and α_{s2}(1-21) [[4]](SEQ ID NO: 4) are preferred. The flanking sequences may optionally be modified by deletion, addition or conservative substitution of one or more residues. The amino acid composition and sequence of the flanking region are not critical as long as the conformation of the peptide is maintained and that all phosphoryl and carboxyl groups interacting with calcium ions are maintained as the preferred flanking regions appear to contribute to the structural action of the motif.

Page 12 paragraph 2.

A 10% w/v casein (Murray Goulburn, Victoria, Australia) or caseinate solution was prepared at pH 8.0 and then digested with trypsin at 0.2% w/w of the casein for 2h at 50°C with the pH controlled to 8.0 ± 0.1 by NaOH addition. After digestion the solution was adjusted to pH 4.6 by the addition of HCl and the precipitate removed by centrifugation or microfiltration. However, the solution can also be clarified by microfiltration at pH 8.0 without acidification. The supernatant or microfiltrate was then adjusted to pH 9.0 with NaOH, then $CaCl_2$ (1.6 M) and Na_2HPO_4 (1 M) at pH 9.0 were added slowly (≤ 1% vol per min) with constant agitation with the pH held constant at 9.0 ± 0.1 by NaOH addition. $CaCl_2$ and sodium phosphate were added to the final concentrations of 100 mM and 60 mM respectively. Following the addition of the calcium and phosphate solutions, the solution was microfiltered through a 0.1 or 0.2 μm microfilter (ceramic or organic) to concentrate the solution five fold. The retentate was then diafiltered with one to five volumes of distilled water. The retentate after diafiltration was spray-dried to produce a white powder that was 50% CPP and 40% ACP and residue water. Analysis of the CPP of the CPP-ACP complex by reversed-phase HPLC, sequence analysis and mass spectrometry revealed that the only peptides that are capable of stabilizing the amorphous calcium phosphate and retained during the microfiltration and diafiltration are Bos α_{s1}-casein X-5P (f59-79) [[1]](SEQ ID NO: 1), Bos β-casein X-4P (fl-25) [[2]](SEQ ID NO: 2), Box α_{s2}-casein X-4P (f46-70) [[3]](SEQ ID NO: 3) and Bos α_{s2}-casein X-4P (f1-21) [[4]](SEQ ID NO: 4) and truncated and heat modified forms of these peptides.

Page 13-14 paragraph 4.

Casein phosphopeptides containing the Ser(P) cluster, i.e. the core sequence motif Ser(P)-Ser(P)-Ser(P)-Glu-Glu-(SEQ ID NO: 5), have a marked ability to stabilize calcium phosphate in solution. Solutions containing 0.1% w/v α_{s1}(59-79) [[1]](SEQ ID NO: 1) at various pH, calcium and phosphate concentrations, but constant ionic strengths were used to characterize the peptide's interaction with calcium phosphate. The peptide was found to maximally bind 24 Ca and 16 Pi per molecule as shown in Table 1.

Page 14 paragraph 1.

The ion activity products for the various calcium phosphate phases [hydroxyapatite (HA); octacalcium phosphate (OCP); tricalcium phosphate (TCP); amorphous calcium phosphate (ACP); and dicalcium phosphate dihydrate (DCPD) were determined from the free calcium and phosphate concentrations at each pH using a computer program that calculates the ion activity coefficients through the use of the expanded Debye-Hückel equation and takes into account the ion pairs $CaHPO_4^{\circ}$, $CaH_2PO_4^{+}$, $CaPO_4^{-}$ and $CaOH^{+}$ the dissociation of H_3PO_4 and H_2O and the ionic strength. The only ion activity product that significantly correlated with calcium phosphate bound to the peptide independently of pH was that corresponding to ACP $[Ca_3(PO_4)_{1.87}(HPO_4)_{.02}\chi H_2O]$ indicating that this is the phase stabilized by α_{s1}(59-79) SEQ ID NO: 1. The peptide α_{s1}(59-79) (SEQ ID NO: 1) binds to forming ACP clusters producing a metastable solution preventing ACP growth to the critical size required for nucleation and precipitation. The binding of α_{s1}(59-79) (SEQ ID NO: 1) to ACP results in the formation of colloidal complexes with the unit formula [α_{s1}(59-79)(SEQ ID NO: 1)$(ACP)_8]_n$ where n is equal to or greater than one. It is likely that the predominant form is n = 6 as α_{s1}(59-79) (SEQ ID NO: 1) cross-linked with glutaraldehyde in the presence of ACP runs as a hexamer on polyacrylamide gel electrophoresis. Interestingly, the synthetic octapeptide α_{s1}(63-70) AcGlu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-GluNHMe (SEQ ID NO: 6) only binds 12 Ca and 8 Pi per molecule i.e. $(ACP)_4$ and the synthetic peptides corresponding to the N-terminus α_{s1}(59-63), Gln-Met-Glu-Ala-Glu (SEQ ID NO: 7) and the C-terminus α_{s1}(71-78), Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln (SEQ ID NO: 8) of

α_{s1}(59-79) did not bind calcium phosphate as shown in Table 1. These results indicate that conformational specificity is essential for full ACP binding.

Page 15 paragraph 2.

We have demonstrated medium- and long-range nuclear Overhauser enhancements (nOes) in 2D ^{1}H NMR spectra of α_{s1}(59-79) [[1]](SEQ ID NO: 1) in the presence of Ca^{2+} indicating a conformational preference. Two structured regions were identified. Residues Val72 to Val76 are implicated in a ß-turn conformation. Residues Glu61 to Ser(P)67, which extend over part of the Ser(P) cluster motif –Ser(P)-Ser(P)-Ser(P)-Glu-Glu- (SEQ ID NO: 5) are involved in a loop-type structure. 2D NMR studies on ß-casein(1-25) (SEQ ID NO: 2) in the presence of calcium have shown a medium range nOe in the –Ser(P)^{17}-Ser(P)-Ser(P)-Glu-Glu^{21}- (SEQ ID NO: 5) motif region between the CαH of Ser(P)^{18} and NH of Blu^{20}. Further medium range nOes include one between the CαH of Ser^{22} and NH of Thr^{24}. Evidence from the ^{1}H NMR spectra of α_{s2}-casein(1-21) [4] have shown that several residues including those around the –Ser(P)-Ser(P)-Ser(P)-Glu-Glu- (SEQ ID NO: 5) are perturbed. Furthermore, there are medium range nOes between NH of Ser(P)^8 and NH of GLU^{10}. This is yet another example of a medium range nOe in the –Ser(P)-Ser(P)-Ser(P)-Glu-Glu- (SEQ ID NO: 5) motif. Other examples of medium range nOes include that between the NH of Ile^{14} and NH of Ser(P)^{16}.

Page 16 paragraph 1.

In summary the NMR data indicates that preferred conformations exist for these peptides in the presence of calcium ions. Molecular modeling of both α_{s1}(59-79) (SEQ ID NO: 1) and ß(1-25) (SEQ ID NO: 2) using the constraints derived from the NMR spectroscopy have indicated that the peptides adopt conformations that allow both glutarnyl and phosphoseryl side chains of the cluster motif –Ser(P)-Ser(P)-Ser(P)-Glu-Glu (SEQ ID NO: 5) to interact collectively with calcium ions of the ACP.

Page 16 paragraph 2.

The relationship between CPP structure and interaction with amorphous calcium phosphate was investigated using a series of synthetic peptide homologues and

analogues indicated in Table 1. These studies showed that the cluster sequence-Ser(*P*)-Ser(*P*)-Ser(*P*)-Glu-Glu- (SEQ ID NO: 5) was mainly responsible for the interaction with ACP and that all three contiguous Ser(*P*) residues are required for maximal interaction with ACP.

Page 17, Table 1.

TABLE 1.

Calcium Phosphate Binding by CPP and Synthetic Homologues and Analogues

	V_{ca} mol/mol	V_{Pi} mol/mol	Ca/P
(SEQ ID NO: 5)ΣΣΣEE	9	6	1.5
(SEQ ID NO: 9)SΣΣEE	2	1	2.0
(SEQ ID NO: 10)EΣΣEE	2	1	2.0
(SEQ ID NO: 11)DΣΣEE	2	1	2.0
(SEQ ID NO: 12)θθθEE	9	6	1.5
(SEQ ID NO: 13)SθθEE	2	1	2.0
(SEQ ID NO: 14)AΣAE	0	0	
(SEQ ID NO: 15)IAΣAEA	0	0	
(SEQ ID NO: 16)EAIAΣAEA	0	0	
(SEQ ID NO: 17)AΣAΣAE	0	0	
(SEQ ID NO: 18)AΣAΣAΣAE	2	1	1.5
(SEQ ID NO: 19)AΣAΣAΣAΣAE	6	4	1.5
(SEQ ID NO: 1)α_{s1}(59-79) QMEAEΣIΣΣΣEEIVPNΣVEQK	24	16	1.5
(SEQ ID NO: 6)α_{s1}(63-70) EΣIΣΣΣEE	12	8	1.5
(SEQ ID NO: 5)α_{s1}(66-70) ΣΣΣEE	9	6	1.5
(SEQ ID NO: 8)α_{s1}(71-78) IVPNΣVEQ[K]	0	0	
(SEQ ID NO: 7)α_{s1}(59-63) QMEAE	0	0	
(SEQ ID NO: 2)β(1-25) RELEELNVPGEIVEΣLΣΣΣEESITR	24	16	1.5
(SEQ ID NO: 20)β(14-21) EΣLΣΣΣEE	12	8	1.5

Σ = Ser(*P*), θ = Thr(*P*), E = Glu, D = Asp, S = Ser, A = Ala, I = Ile, Q = Gln, M = Met, V = Val, P = Pro, K = Lys, L = Leu, T = Thr, G = Gly and R = Arg.

Page 19, Table 2.

TABLE 2.

CPP and Synthetic Peptide binding to HA at 37°C

	K ml/ μmol	N μmol/ m^2	Molecular Area nm^2
(SEQ ID NO: 1)α_{s1} (59-79) QMEAEΣIΣΣΣEEIVPNΣVEQK	415	0.35	4.75
(SEQ ID NO: 6)α_{s1} (63-70) EΣIΣΣΣEE	10,370	0.47	3.56
(SEQ ID NO: 5)α_{s1} (66-70) ΣΣΣEE	12,845	0.52	3.27
(SEQ ID NO: 8)α_{s1} (71-78) IVPNΣVEQ[K]	-	-	-
(SEQ ID NO: 7)α_{s1} (59-63) QMEAE	-	-	-
(SEQ ID NO: 5)ΣΣΣEE	12,845	0.52	3.27
(SEQ ID NO: 10)EΣΣEE	1,513	0.96	1.74
(SEQ ID NO: 11)DΣΣEE	6,579	0.81	2.04
(SEQ ID NO: 12)θθθEE	12,234	0.51	3.27
(SEQ ID NO: 21)TθθEE	1,013	0.55	3.03
(SEQ ID NO: 22)θTθEE	837	0.44	3.77
(SEQ ID NO: 23)θθTEE	1,799	0.46	3.61

Σ = Ser(*P*), θ = Thr(*P*)

Page 20, paragraph 2.

We have also studied the docking of the peptide Ser(*P*)- Ser(*P*)- Ser(*P*)-Glu-Glu- (SEQ ID NO: 5) onto three crystallographic planes of HA, {100}, {010} and {001} using computer simulation techniques and the unit cell coordinates of synthetic HA. These simulation studies revealed that the peptide - Ser(*P*)- Ser(*P*)- Ser(*P*)-Glu-Glu- (SEQ ID NO: 5) is more likely to the {100} surface, followed by the {010} surface. The Ser(*P*)-cluster motif can therefore bind to both {100} and {010} surfaces thus allowing deposition of calcium, phosphate and hydroxyl ions on the {100} surface enabling

growth of the HA crystal along the *c*-axis only. These results therefore can know explain the *c*-axis growth of HA crystals in enamel and dentine. Detailed examination of the computer simulation data shows that the - Ser(*P*)- Ser(*P*)- Ser(*P*)-Glu-Glu- (SEQ ID NO: 5) conformer with the greatest relative binding energy is positioned on the HA surface such that the carboxyl groups of the glutamyl residues and the phosphoryl groups of the phosphoseryl residues are in proximity to the HA surface with maximal contact between these groups and surface calcium atoms.

Page 21, paragraph 2.

Two exposures of the CPP-ACP solution per day to the right pair of enamel slabs for 12 subjects produced a 51% ± 19% reduction in enamel mineral loss relative to the left-side, control enamel. The plaque exposed to the CPP-ACP solution contained 78 ± 22 μmol/g calcium, 52 ± 25 μmol/g P_i and 2.4 ± 0.7 mg/g CPP compared with 32 ± 12 μmol/g calcium and 20 ± 11 μmol/g P_i in the control plaque. The level of the CPP was determined by competitive ELISA using an antibody that recognizes both α_{s1}(59-79) (SEQ ID NO: 1) and β(1-25) (SEQ ID NO: 2). Electron micrographs of immunocytochemically stained sections of the plaque revealed localization of the peptide predominantly on the surface of microorganisms but also in the extracellular matrix.

Marked up rewritten claims:

1. **(Amended)** A stable calcium phosphate complex including phosphopeptide stabilized calcium fluoride phosphate or a derivative thereof wherein said phosphopeptide includes the amino acid sequence Ser(*P*)-Ser(*P*)-Ser(*P*)-Glu-Glu (SEQ ID NO: 5).

4. **(Amended)** A complex according to claim 3 wherein said phosphopeptide includes an amino acid sequence selected from any one of:

[1](SEQ ID NO: 1) Gln^{59}-Met-Glu-Ala-Gelu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys^{79}. α_{s1}(59-79)

[2](SEQ ID NO: 2) Arg[1]-Glu-Le8-Glu-lu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg[25]. β(I-25)

[3](SEQ ID NO: 3) Asn[46]-Ala-Asn-Glu-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys[70]. α_{s2}(46-70)

[4](SEQ ID NO: 4) Lys[1]-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys[21]. α_{s2}(1-21)

5. **(Amended)** A complex according to claim 3 wherein said phosphopeptide includes the amino acid sequence (SEQ ID NO: 1):

Gln[59]-Met-Glu-Ala-Gelu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys[79]. α_{s1}(59-79)

7. **(Amended)** A stable soluble alkaline calcium phosphate [complex] comprising phosphopeptide-stabilized amorphous calcium phosphate or a derivative thereof wherein said phosphopeptide includes the amino acid sequence Ser*(P)*-Ser*(P)*-Ser*(P)*-Glu-Glu and said amorphous calcium phosphate or the derivative thereof is alkaline.

9. **(Amended)** A complex according to claim 8 further including [HPO_4] $HPO_4^{(2-)}$.

10. **(Amended)** A complex according to claim 9 wherein said phosphopeptide includes an amino acid sequence selected from any one of:

[1](SEQ ID NO: 1) Gln[59]-Met-Glu-Ala-Gelu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys[79]. α_{s1}(59-79)

[2](SEQ ID NO: 2) Arg^{1}-Glu-Le8-Glu-lu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg^{25}. β(I-25)

[3](SEQ ID NO: 3) Asn^{46}-Ala-Asn-Glu-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys^{70}. α_{s2}(46-70)

[4](SEQ ID NO: 4) Lys^{1}-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys^{21}. α_{s2}(1-21)

11. **(Twice Amended)** A complex according to claim 9 wherein said phosphopeptide includes the amino acid sequence (SEQ ID NO: 1):

Gln^{59}-Met-Glu-Ala-Gelu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys^{79}. α_{s1}(59-79)

12. **(Twice Amended)** A complex according to claim 11 having the formula $[(PP)(CP_8)]_n$ where n is equal to or greater than 1, wherein "PP" represents a phosphopeptide, and "CP" represents calcium phosphate.

13. **(Twice Amended)** A complex according to claims 12 having the formula $[(PP)(CP_8)]_6$ wherein "PP" represents a phosphopeptide, and "CP" represents calcium phosphate.